

FILE 'MEDLINE' ENTERED AT 16:13:35 ON 25 JAN 2000

L11 ANSWER 1 OF 1 MEDLINE

AN 96071635 MEDLINE

DN 96071635

TI \*\*\*Discovery\*\*\* of \*\*\*betulinic\*\*\* \*\*\*acid\*\*\* as a selective inhibitor of human melanoma that functions by induction of apoptosis.

AU Pisha E; Chai H; Lee I S; Chagwedera T E; Farnsworth N R; Cordell G A; Beecher C W; Fong H H; Kinghorn A D; Brown D M; et al

CS Department of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, University of Illinois at Chicago 60612, USA.

NC U01 CA 52956 (NCI)

SO NATURE MEDICINE, (1995 Oct) 1 (10) 1046-51.

Journal code: CG5. ISSN: 1078-8956.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199603

AB As a result of bioassay-guided fractionation, betulinic acid, a pentacyclic triterpene, was identified as a melanoma-specific cytotoxic agent. In follow-up studies conducted with athymic mice carrying human melanomas, tumour growth was completely inhibited without toxicity. As judged by a variety of cellular responses, antitumour activity was mediated by the induction of apoptosis. Betulinic acid is inexpensive and available in abundant supply from common natural sources, notably the bark of white birch trees. The compound is currently undergoing preclinical development for the treatment or prevention of malignant melanoma.

Req 1/25

09/089894

=> file ca

=> e betulinol

E1 3 BETULINE/BI  
E2 518 BETULINIC/BI  
E3 40 --> BETULINOL/BI  
E4 7 BETULINS/BI  
E5 2 BETULINUM/BI  
E6 54 BETULINUS/BI  
E7 2 BETULINYL/BI  
E8 1 BETULISA/BI  
E9 3 BETULLA/BI  
E10 1 BETULO/BI  
E11 11 BETULOIDES/BI  
E12 1 BETULOL/BI

=> s el-e4

3 BETULINE/BI  
518 BETULINIC/BI  
40 BETULINOL/BI  
7 BETULINS/BI  
L1 562 (BETULINE/BI OR BETULINIC/BI OR BETULINOL/BI OR BETULINS/BI)

=> s ether# or diether#

282088 ETHER#  
1746 DIETHER#  
L2 282701 ETHER# OR DIETHER#

=> s l1(10a)l2

L3 6 L1(10A)L2

=> d bib,kwic

L3 ANSWER 1 OF 6 CA COPYRIGHT 2000 ACS  
AN 131:226125 CA

TI Zatriol. A new aromatic constituent from Zataria multiflora  
 AU Ali, Muhammad Shaiq; Saleem, Muhammad; Ahmad, Viqar Uddin  
 CS H. E. J. Research Institute Chemistry, Univ. Karachi, Karachi, 75270, Pak.  
 SO Z. Naturforsch., B: Chem. Sci. (1999), 54(6), 807-810  
 CODEN: ZNBSEN; ISSN: 0932-0776  
 PB Verlag der Zeitschrift fuer Naturforschung  
 DT Journal  
 LA English  
 AB . . . isolated from the hexane sol. part of a Lamiaceous plant Zataria multiflora. Zatriol and some known constituents, p-cymene, thymol, thymol methyl- \*\*\*ether\*\*\*, .beta.-sitosterol, stigmasterol, oleanolic acid, \*\*\*betulinic\*\*\* acid, and hexadecanoic acid were also isolated from the same source. Structures of the isolated constituents were elucidated with the. . .

=> d bib,kwic 2-6

L3 ANSWER 2 OF 6 CA COPYRIGHT 2000 ACS

AN 129:260594 CA

TI Process for the extraction of betulinic acid from the bark of Platanus acerifolia using middle-polar extraction solvents

IN Draeger, Birgit; Neubert, Reinhard; Galgon, Tino; Wohlrab, Wolfgang

PA Martin-Luther-Universitaet Halle-Wittenberg, Germany

SO Ger. Offen., 2 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19713768	A1	19981008	DE 1997-19713768	19970403

PI DE 19713768 A1 19981008 DE 1997-19713768 19970403  
 PRAI DE 1997-19713768 19970403

IT 60-29-7, Diethyl \*\*\*ether\*\*\*, uses 67-66-3, Trichloromethane, uses 75-09-2, Dichloromethane, uses

RL: NUU (Nonbiological use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)

(extn. solvent; process for the extn. of \*\*\*betulinic\*\*\* acid from the bark of Platanus acerifolia using middle-polar extn. solvents)

L3 ANSWER 3 OF 6 CA COPYRIGHT 2000 ACS

AN 104:17690 CA

TI Chemistry of Euphorbiaceae. Part III. Isolation of lupane group triterpenes from Givotia rottleriformis Griff

AU Reddy, K. Dharma; Reddy, R. Prasad; Raj, S. K. Ram; Ravindranath, A.; Sundararamaiah, T.

CS Dep. Chem., Nizam Coll., Hyderabad, 500 001, India

SO J. Indian Chem. Soc. (1985), 62(5), 411

CODEN: JICSAH; ISSN: 0019-4522

DT Journal

LA English

AB An \*\*\*ether\*\*\* ext. of *G. rottleriformis* bark afforded \*\*\*betulinic\*\*\* acid, lupeol, and betulin. Identification was made by co-chromatog. (TLC) and from spectral data.

L3 ANSWER 4 OF 6 CA COPYRIGHT 2000 ACS

AN 92:211825 CA

TI The chemical constituents of *Symplocos racemosa* Roxb

AU De Silva, L. B.; De Silva, U. L. L.; Mahendran, M.

CS Med. Res. Inst., Colombo, 8, Sri Lanka

SO J. Natl. Sci. Counc. Sri Lanka (1979), 7(1), 1-3

CODEN: JNSCBH; ISSN: 0300-9254

DT Journal

LA English

AB Petroleum ether and \*\*\*ether\*\*\* exts. of *S. racemosa* afforded a high yield of \*\*\*betulinic\*\*\* acid with smaller amts. of acetyloleanolic and oleanolic acids. The cold MeOH ext. yielded ellagic acid. The structures were detd.. . .

L3 ANSWER 5 OF 6 CA COPYRIGHT 2000 ACS

AN 84:2225 CA

TI Triterpenoids of *Callistemon lanceolatus* leaves

AU Varma, R. S.; Parthasarathy, M. R.

CS Dep. Chem., Univ. Delhi, Delhi, India

SO Phytochemistry (1975), 14(7), 1675-6

CODEN: PYTCAS

DT Journal

LA English

AB Air-dried and powd. leaves of *C. lanceolatus* exhaustively extd. with petroleum \*\*\*ether\*\*\* (60-80.degree.), Me<sub>2</sub>CO, and EtOH yielded sitosterol, erythrodiol, betulin, \*\*\*betulinic\*\*\* acid, ursolic acid, and 2.alpha.-hydroxyursolic acid.

L3 ANSWER 6 OF 6 CA COPYRIGHT 2000 ACS

AN 68:19514 CA

TI Brazilian Guttiferae. X. Triterpene constituents of *Clusia*

AU Clemente de Araujo, Hugo; Mahajan, J. R.; Gottlieb, Otto R.; Magalhaes, Mauro T.

CS Univ. Federal Minas Gerais, Belo Horizonte, Brazil

SO Ann. Acad. Brasil. Cienc. (1966), 38(3-4), 429-30

DT Journal

LA Portuguese

AB The trunk wood of a *Clusia* species was shown to contain .beta.-sitosterol, .beta.-amyrin, and \*\*\*betulinic\*\*\* acid by elution with C<sub>6</sub>H<sub>6</sub>, C<sub>6</sub>H<sub>6</sub>-CHCl<sub>3</sub>, and petroleum \*\*\*ether\*\*\*, resp. The wood was previously

washed with 3% aq. NaOH to eliminate acid material.

=> d history

(FILE 'HOME' ENTERED AT 15:11:55 ON 25 JAN 2000)

FILE 'CA' ENTERED AT 15:11:59 ON 25 JAN 2000

E BETULINOL

L1 562 S E1-E4  
L2 282701 S ETHER# OR DIETHER#  
L3 6 S L1(10A)L2

=> s l1 or betulonic

42 BETULONIC

L4 589 L1 OR BETULONIC

=> s aldehyde#

L5 87803 ALDEHYDE#

=> s l4(10a)l5

L6 6 L4(10A)L5

=> d bib,kwic 1-6

L6 ANSWER 1 OF 6 CA COPYRIGHT 2000 ACS

AN 130:52599 CA

TI synthesis and antitumor activity of betulinal derivatives and monoclonal antibody conjugates

IN Bomshteyn, Arkadiy L.; Rathnam, Premila; Saxena, Brij B.

PA Cornell Research Foundation, Inc., USA

SO PCT Int. Appl., 56 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9855497	A1	19981210	WO 1998-US11456	19980603

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,  
 UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,  
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,  
 CM, GA, GN, ML, MR, NE, SN, TD, TG  
 AU 9878135 AI 19981221 AU 1998-78135 19980603  
 PRAI US 1997-48621 19970604  
 WO 1998-US11456 19980603  
 OS MARPAT 130:52599  
 IT 1721-69-3P 4439-98-9P, \*\*\*Betulonic\*\*\* \*\*\*aldehyde\*\*\*  
 217312-62-4DP, monoclonal antibody conjugate 217312-62-4P  
 217312-63-5DP, monoclonal antibody conjugate 217312-63-5P  
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic  
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)  
 (synthesis and antitumor activity of \*\*\*betulinol\*\*\* derivs. and  
 monoclonal antibody conjugates)

L6 ANSWER 2 OF 6 CA COPYRIGHT 2000 ACS

AN 122:310746 CA

TI Terpenoids, alkaloids and coumarins from *Boronia inornata* and *Boronia  
 gracilipes*

AU Ahsan, Monira; Armstrong, James A.; Gray, Alexander I.; Waterman, Peter G.

CS Dep. Pharm. Sci., Univ. Strathclyde, Glasgow, G1 1XW, UK

SO Phytochemistry (1995), 38(5), 1275-8

CODEN: PYTCAS; ISSN: 0031-9422

DT Journal

LA English

AB Aerial parts and roots of *Boronia inornata* yielded the sesquiterpenes spathulenol and  
 1(10),5-germacradien-4-ol, the triterpenes moronic acid, the new moronic \*\*\*aldehyde\*\*\*,  
 \*\*\*betulonic\*\*\* acid and lupeol, the alkaloids dictamnine, evolitrine, isodictamnine and hordenine, and  
 8-(3,7-dimethyl-2,6-octadienyl)-7-hydroxycoumarin. A second sample of B.

*inornata* gave the. . . protolimonoids niloticin and piscidinol-A in addn. to all those compds. noted  
 above. B. *gracilipes* yielded spathulenol, rutin and the triterpenes \*\*\*betulonic\*\*\* acid,  
 \*\*\*betulonic\*\*\* \*\*\*aldehyde\*\*\*, oleanonic acid, 3-epioleanonic acid and oleanic \*\*\*aldehyde\*\*\*.

Results are now available for

investigations of species belonging to all three of the sections of  
*Boronia* and the distribution. . .

IT 153-18-4 484-29-7, Dictamnine 484-74-2, Isodictamnine 523-66-0, Evolitrine 539-15-1,  
 Hordenine 545-47-1, Lupeol 4439-98-9, \*\*\*Betulonic\*\*\* \*\*\*aldehyde\*\*\* 4481-62-3, Betulonic  
 acid 6713-27-5, Moronic acid 6750-60-3, Spathulenol 17990-42-0, Oleanonic acid 23660-05-1  
 25499-90-5, 3-Epioleanolic acid 33608-08-1

74841-87-5 100198-09-2, Piscidinol-A 115404-57-4, Niloticin

RL: BOC (Biological occurrence); BIOL (Biological study); OCCU  
 (Occurrence)

(from *Boronia inornata* and B. *gracilipes*)

L6 ANSWER 3 OF 6 CA COPYRIGHT 2000 ACS

AN 121:276719 CA

TI Potential allelopathic lupane triterpenes from bioactive fractions of  
*Melilotus messanensis*

AU Macias, Francisco A.; Simonet, Ana M.; Esteban, M. Dolores

CS Fac. Ciencias, Univ. Cadiz, Cadiz, 11510, Spain

SO Phytochemistry (1994), 36(6), 1369-79

CODEN: PYTCAS; ISSN: 0031-9422

DT Journal

LA English

AB . . . *messanensis* (sweet clover) afforded, from the medium polar bioactive fractions, in addn. to the known lupane triterpenes lupeol, betulin, betulin \*\*\*aldehyde\*\*\*, and \*\*\*betulinic\*\*\* acid, the new norlupane messagenin (I, 30-norlupane-3.beta.,28-diol-20-one) which have been tested as allelochems. Structures and their stereochems. were elucidated by. . .

L6 ANSWER 4 OF 6 CA COPYRIGHT 2000 ACS

AN 114:98300 CA

TI Composition of the triterpene fraction of outer bark extracts of *Betula pendula* and *Betula pubescens*

AU Pokhilo, N. D.; Makhnev, A. K.; Demenkova, L. I.; Uvarova, N. I.

CS Tikhookean. Inst. Bioorg. Khim., Vladivostok, USSR

SO Khim. Drev. (1990), (6), 74-7

CODEN: KHDRDQ; ISSN: 0201-7474

DT Journal

LA Russian

AB . . . in Mar.-Dec., contained 31.9-42.1% CHCl<sub>3</sub>-ext. which contained betulin (I) 15.3-67.6, lupeol (II) 1.15-2.91, betulinic (III) + oleanolic acids (1:2-7:2) 5.7-21.2, \*\*\*betulinic\*\*\* + oleanolic \*\*\*aldehydes\*\*\* (1:2-2:1) traces-1.43, oleanolic acid acetate (IV) 0.58-3.9, erythrodiol 1.0-3.2, and .beta.-sitosterol traces-0.74%. *B. pendula* bark contained 31.8-33.0% ext. which contained. . .

IT 83-46-5 508-02-1 545-48-2, Erythrodiol 13159-28-9, \*\*\*Betulinic\*\*\* \*\*\*aldehyde\*\*\* 17020-22-3, Oleanolic aldehyde

RL: BIOL (Biological study)

(from *Betula pubescens* bark)

L6 ANSWER 5 OF 6 CA COPYRIGHT 2000 ACS

AN 106:153022 CA

TI The composition of the outer bark of *Betula mandschurica*

AU Kochergina, T. Yu.; Malinovskaya, G. V.; Pokhilo, N. D.; Denisenko, V. A.; Uvarova, N. I.

CS Tikhookean. Inst. Bioorg. Khim., Vladivostok, USSR

SO Khim. Prir. Soedin. (1986), (5), 647-8

CODEN: KPSUAR; ISSN: 0023-1150

DT Journal

LA Russian

AB . . . were isolated from the outer bark of *B. mandschurica*, including lupeol, oleanolic acid acetate, .beta.-sitosterol, betulin, oleanolic acid, betulin caffeate, \*\*\*betulinic\*\*\* \*\*\*aldehyde\*\*\*, and 3.beta.-acetyl-11.alpha.,12.alpha.-epoxyolean-13,28-olide. The latter 3 were identified by physicochem. and spectral characteristics.

IT 83-46-5, .beta.-Sitosterol 473-98-3, Betulin 508-02-1, Oleanolic acid 545-47-1, Lupeol 4339-72-4, Oleanolic acid acetate 13159-28-9, \*\*\*Betulinic\*\*\* \*\*\*aldehyde\*\*\* 89130-86-9

RL: BIOL (Biological study)  
(of *Betula mandschurica* outer bark)

L6 ANSWER 6 OF 6 CA COPYRIGHT 2000 ACS

AN 95:150946 CA

TI Triterpenes in organ pipe cactus

AU Kircher, Henry W.

CS Dep. Nutr. Food Sci., Univ. Arizona, Tucson, AZ, 85721, USA

SO Phytochemistry (1980), 19(12), 2707-12

CODEN: PYTCAS; ISSN: 0031-9422

DT Journal

LA English

AB . . . their structures were detd. by spectral methods. They were arranged in a biosynthetic scheme based on the degree of oxidn.

\*\*\*Betulinic\*\*\* \*\*\*aldehyde\*\*\* I (R = OH, R1 = R3 = H, R2 = CHO) and oleanolic aldehydes II (R = OH, R1. . .

ST *Stenocereus* lupene oleanene structure; \*\*\*betulinic\*\*\* \*\*\*aldehyde\*\*\* ; oleanolic aldehyde

=> s ?peptide? or protein? or antibody or antibodies

387437 ?PEPTIDE?

1235224 PROTEIN?

187370 ANTIBODY

196212 ANTIBODIES

L7 1569404 ?PEPTIDE? OR PROTEIN? OR ANTIBODY OR ANTIBODIES

=> d history

(FILE 'HOME' ENTERED AT 15:11:55 ON 25 JAN 2000)

FILE 'CA' ENTERED AT 15:11:59 ON 25 JAN 2000

E BETULINOL

L1 562 S E1-E4

L2 282701 S ETHER# OR DIETHER#



L3 6 S L1(10A)L2  
 L4 589 S L1 OR BETULONIC  
 L5 87803 S ALDEHYDE#  
 L6 6 S L4(10A)L5  
 L7 1569404 S ?PEPTIDE? OR PROTEIN? OR ANTIBODY OR ANTIBODIES

=> s l4(P)l7

L8 9 L4(P)L7

=> d bib,kwic

L8 ANSWER 1 OF 9 CA COPYRIGHT 2000 ACS

AN 131:111059 CA

TI \*\*\*Betulinic\*\*\* acid-induced apoptosis in glioma cells: a sequential requirement for new \*\*\*protein\*\*\* synthesis, formation of reactive oxygen species, and caspase processing

AU Wick, Wolfgang; Grimm, Cornelia; Wagenknecht, Bettina; Dichgans, Johannes; Weller, Michael

CS Laboratory of Molecular Neuro-Oncology, Department of Neurology, School of Medicine, University of Tübingen, Tübingen, Germany

SO J. Pharmacol. Exp. Ther. (1999), 289(3), 1306-1312

CODEN: JPETAB; ISSN: 0022-3565

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

LA English

TI \*\*\*Betulinic\*\*\* acid-induced apoptosis in glioma cells: a sequential requirement for new \*\*\*protein\*\*\* synthesis, formation of reactive oxygen species, and caspase processing

AB \*\*\*Betulinic\*\*\* acid (BA), a pentacyclic triterpene, is an exptl. cytotoxic agent for malignant melanoma. Here, we show that BA triggers apoptosis in five human glioma cell lines. BA-induced apoptosis requires new \*\*\*protein\*\*\*, but not RNA, synthesis, is independent of p53, and results in p21 \*\*\*protein\*\*\* accumulation in the absence of a cell cycle arrest. BA-induced apoptosis involves the activation of caspases that cleave poly-(ADP ribose)polymerase. . . pairs of the CD95/CD95 ligand family do not mediate BA-induced caspase activation. BA enhances the levels of BAX and BCL-2 \*\*\*proteins\*\*\* but does not alter the levels of BCL-xS or BCL-xL. Ectopic expression of BCL-2 prevents BA-induced caspase activation, DNA fragmentation, . . . that are essential for BA-triggered cell death. The generation of reactive oxygen species is blocked by BCL-2 and requires new \*\*\*protein\*\*\* synthesis but is unaffected by caspase inhibitors, suggesting that BA toxicity sequentially involves new \*\*\*protein\*\*\* synthesis, formation of reactive oxygen species, and activation of crm-A-insensitive caspases.

ST \*\*\*betulinic\*\*\* acid apoptosis glioma \*\*\*protein\*\*\* synthesis;

- caspase oxygen species \*\*\*betulinic\*\*\* acid glioma
- IT Cell cycle  
 (arrest; \*\*\*betulinic\*\*\* acid-induced apoptosis in glioma cells:  
 role of \*\*\*protein\*\*\* synthesis, reactive oxygen species, and  
 caspase)
- IT Apoptosis  
 Glioma inhibitors  
 Translation (genetic)  
 ( \*\*\*betulinic\*\*\* acid-induced apoptosis in glioma cells: role of  
 \*\*\*protein\*\*\* synthesis, reactive oxygen species, and caspase)
- IT Bax \*\*\*protein\*\*\*  
 Bcl-x \*\*\*protein\*\*\*  
 Reactive oxygen species  
 bcl-2 \*\*\*protein\*\*\*  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 ( \*\*\*betulinic\*\*\* acid-induced apoptosis in glioma cells: role of  
 \*\*\*protein\*\*\* synthesis, reactive oxygen species, and caspase)
- IT Fas ligand  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 ( \*\*\*betulinic\*\*\* acid-induced apoptosis in glioma cells: role of  
 \*\*\*protein\*\*\* synthesis, reactive oxygen species, and caspase)
- IT p21CIP1/WAF1 \*\*\*protein\*\*\*  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 ( \*\*\*betulinic\*\*\* acid-induced apoptosis in glioma cells: role of  
 \*\*\*protein\*\*\* synthesis, reactive oxygen species, and caspase)
- IT p53 ( \*\*\*protein\*\*\* )  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 ( \*\*\*betulinic\*\*\* acid-induced apoptosis in glioma cells: role of  
 \*\*\*protein\*\*\* synthesis, reactive oxygen species, and caspase)
- IT 472-15-1, \*\*\*Betulinic\*\*\* acid  
 RL: BAC (Biological activity or effector, except adverse); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 ( \*\*\*betulinic\*\*\* acid-induced apoptosis in glioma cells: role of  
 \*\*\*protein\*\*\* synthesis, reactive oxygen species, and caspase)
- IT 186322-81-6, Caspase  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 ( \*\*\*betulinic\*\*\* acid-induced apoptosis in glioma cells: role of  
 \*\*\*protein\*\*\* synthesis, reactive oxygen species, and caspase)
- IT 9055-67-8, Poly-(ADP ribose)polymerase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 ( \*\*\*betulinic\*\*\* acid-induced apoptosis in glioma cells: role of  
 \*\*\*protein\*\*\* synthesis, reactive oxygen species, and caspase)

=> d bib,kwic 2-9

LS ANSWER 2 OF 9 CA COPYRIGHT 2000 ACS

AN 130:52599 CA

TI- synthesis and antitumor activity of \* \*betulinol\*\*\* derivatives and  
monoclonal \*\*\*antibody\*\*\* conjugates

IN Bomshteyn, Arkadiy L.; Rathnam, Premila; Saxena, Brij B.

PA Cornell Research Foundation, Inc., USA

SO PCT Int. Appl., 56 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 9855497	A1	19981210	WO 1998-US11456	19980603
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W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,  
DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,  
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,  
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,  
UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,  
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,  
CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9878135	A1	19981221	AU 1998-78135	19980603
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PRAI US 1997-48621 19970604

WO 1998-US11456 19980603

OS MARPAT 130:52599

TI synthesis and antitumor activity of \*\*\*betulinol\*\*\* derivatives and  
monoclonal \*\*\*antibody\*\*\* conjugates

AB Syntheses of \*\*\*betulinol\*\*\* derivs. (I) (X, Y1 = independently OH,  
alkoxy, alkanoyloxy, - \*\*\*peptide\*\*\* -NHNH-C(O)- \*\*\*antibody\*\*\* -OH  
moiety) and \*\*\*betulinol\*\*\* - \*\*\*antibody\*\*\* conjugates (II) (A1 =  
I- \*\*\*peptide\*\*\* -NHN=CH, I- \*\*\*peptide\*\*\* -NHNH) are disclosed.

ST \*\*\*betulinol\*\*\* \*\*\*peptide\*\*\* monoclonal \*\*\*antibody\*\*\*  
conjugates prepn

IT Antitumor agents

(synthesis and antitumor activity of \*\*\*betulinol\*\*\* derivs. and  
monoclonal \*\*\*antibody\*\*\* conjugates)

IT Monoclonal \*\*\*antibody\*\*\* conjugates

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic  
preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)

(synthesis and antitumor activity of \*\*\*betulinol\*\*\* derivs. and  
monoclonal \*\*\*antibody\*\*\* conjugates)

IT 1721-69-3P 4439-98-9P, \*\*\*Betulonic\*\*\* aldehyde 217312-62-4DP,  
monoclonal \*\*\*antibody\*\*\* conjugate 217312-62-4P 217312-63-5DP,  
monoclonal \*\*\*antibody\*\*\* conjugate 217312-63-5P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis and antitumor activity of **\*\*betulinol\*\*** derivs. and monoclonal **\*\*\*antibody\*\*\*** conjugates)

IT 473-98-3, **\*\*\*Betulinol\*\*\*** 99933-15-0 148134-13-8 148134-13-8D, monoclonal **\*\*\*antibody\*\*\*** conjugate 217312-61-3

RL: RCT (Reactant)

(synthesis and antitumor activity of **\*\*\*betulinol\*\*\*** derivs. and monoclonal **\*\*\*antibody\*\*\*** conjugates)

L8 ANSWER 3 OF 9 CA COPYRIGHT 2000 ACS

AN 129:118645 CA

TL Induction of p53 without increase in p21 WAF1 in betulinic acid-mediated cell death is preferential for human metastatic melanoma

AU Rieber, Manuel; Rieber, Mary Strasberg

CS IVIC, Tumor Cell Biology Lab., Caracas, 1020 A, Venez.

SO DNA Cell Biol. (1998), 17(5), 399-406

CODEN: DCEBE8; ISSN: 1044-5498

PB Mary Ann Liebert, Inc.

DT Journal

LA English

IT Rb **\*\*\*protein\*\*\***

RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)

(cyclins D1 and D3 and phosphorylated Rb decreased in melanoma cells exposed to **\*\*\*betulinic\*\*\*** acid; induction of p53 without increase in p21 WAF1 in **\*\*\*betulinic\*\*\*** acid-mediated cell death is preferential for human metastatic melanoma)

IT p53 ( **\*\*\*protein\*\*\*** )

RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(induction of p53 without increase in p21 WAF1 in **\*\*\*betulinic\*\*\*** acid-mediated cell death is preferential for human metastatic melanoma)

IT p21CIP1/WAF1 **\*\*\*protein\*\*\***

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(induction of p53 without increase in p21 WAF1 in **\*\*\*betulinic\*\*\*** acid-mediated cell death is preferential for human metastatic melanoma)

L8 ANSWER 4 OF 9 CA COPYRIGHT 2000 ACS

AN 128:162486 CA

TI Plant-derived leading compounds for chemotherapy of human immunodeficiency virus (HIV) infection

AU Vlietinck, A. J.; De Bruyne, T.; Apers, S.; Pieters, L. A.

CS Department Pharmaceutical Sciences, University Antwerp, Antwerp, B-2610, Belg.

SO Planta Med. (1998), 64(2), 97-109

CODEN: PLMEAA; ISSN: 0032-0943

PB Georg Thieme Verlag  
 DT Journal; General Review  
 LA English

AB . . . acid derivs.), tannins, and triterpenes (glycyrrhizin and analogs, soyasaponin and analogs). (2) Virus-cell fusion: lectins (mannose- and N-acetylglucosamine-specific) and triterpenes (\*\*\*betulinic\*\*\* acid and analogs). (3) Reverse transcription: alkaloids (benzophenanthridines, protoberberines, isoquinolines, quinolines), coumarins (calanolides and analogs), flavonoids, phloroglucinols, lactones (protolichesterinic acid),. . . (4) Integration: coumarins (3-substituted-4-hydroxycoumarins), depsidones, O-caffeoyl derivs., lignans (arctigenin and analogs), and phenolics (curcumin). (5) Translation: single chain ribosome inactivating \*\*\*proteins\*\*\* (SCRIP's). (6) Proteolytic cleavage (protease inhibition): saponins (ursolic and maslinic acids), xanthones (mangostin and analogs), and coumarins. (7) Glycosylation: alkaloids. . .

L8 ANSWER 5 OF 9 CA COPYRIGHT 2000 ACS

AN 128:43516 CA

TI Betulinic acid triggers CD95 (APO-1/Fas)- and p53-independent apoptosis via activation of caspases in neuroectodermal tumors

AU Fulda, Simone; Friesen, Claudia; Los, Marek; Scaffidi, Carsten; Mier, Walter; Benedict, Mary; Nunez, Gabriel; Krammer, Peter H.; Peter, Marcus E.; Debatin, Klaus-Michael

CS Division of Hematology/Oncology, German Cancer Research Center, University Children's Hospital and Division of Molecular Oncology, Heidelberg, D-69120, Germany

SO Cancer Res. (1997), 57(21), 4956-4964

CODEN: CNREA8; ISSN: 0008-5472

PB American Association for Cancer Research

DT Journal

LA English

AB \*\*\*Betulinic\*\*\* acid (BA), a melanoma-specific cytotoxic agent, induced apoptosis in neuroectodermal tumors, such as neuroblastoma, medulloblastoma, and Ewing's sarcoma, representing the. . . the one previously identified for std. chemotherapeutic drugs. BA-induced apoptosis was independent of CD95-ligand/receptor interaction and accumulation of wild-type p53 \*\*\*protein\*\*\*, but it critically depended on activation of caspases (interleukin 1.beta.-converting enzyme/Ced-3-like proteases). FLICE/MACH (caspase-8), considered to be an upstream protease. . . and the downstream caspase CPP32/YAMA/Apopain (caspase-3) were activated, resulting in cleavage of the prototype substrate of caspases PARP. The broad-spectrum \*\*\*peptide\*\*\* inhibitor benzyloxycarbonyl-Val-Ala-Asp-fluoromethylketone, which blocked cleavage of FLICE and PARP, also completely abrogated BA-triggered apoptosis. Cleavage of caspases was preceded by. . . nuclear fragmentation. This suggested that mitochondrial alterations were

involved in BA-induced activation of caspases. Furthermore, Bax and Bcl-xs, two death-promoting \*\*\*proteins\*\*\* of the Bcl-2 family, were up-regulated following BA treatment. Most importantly, neuroblastoma cells resistant to CD95- and doxorubicin-mediated apoptosis were. . .

IT Bcl-x \*\*\*protein\*\*\*

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
(Bcl-xL; \*\*\*betulinic\*\*\* acid triggers CD95 APO-1/Fas- and p53-independent apoptosis via activation of caspases in neuroectodermal tumors in relation to Bcl-2 family \*\*\*proteins\*\*\* expression and mitochondrial dysfunction and resistance)

IT Bcl-x \*\*\*protein\*\*\*

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
(Bcl-xs; \*\*\*betulinic\*\*\* acid triggers CD95 APO-1/Fas- and p53-independent apoptosis via activation of caspases in neuroectodermal tumors in relation to Bcl-2 family \*\*\*proteins\*\*\* expression and mitochondrial dysfunction and resistance)

IT Sarcoma inhibitors

(Ewing's; \*\*\*betulinic\*\*\* acid triggers CD95 APO-1/Fas- and p53-independent apoptosis via activation of caspases in neuroectodermal tumors in relation to Bcl-2 family \*\*\*proteins\*\*\* expression and mitochondrial dysfunction and resistance)

IT Antitumor agent resistance

Apoptosis

Mitochondria

Neuroblastoma inhibitors

( \*\*\*betulinic\*\*\* acid triggers CD95 APO-1/Fas- and p53-independent apoptosis via activation of caspases in neuroectodermal tumors in relation to Bcl-2 family \*\*\*proteins\*\*\* expression and mitochondrial dysfunction and resistance)

IT Bax \*\*\*protein\*\*\*

Fas antigen

Fas ligand

bcl-2 \*\*\*protein\*\*\*

p53 ( \*\*\*protein\*\*\* )

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
( \*\*\*betulinic\*\*\* acid triggers CD95 APO-1/Fas- and p53-independent apoptosis via activation of caspases in neuroectodermal tumors in relation to Bcl-2 family \*\*\*proteins\*\*\* expression and mitochondrial dysfunction and resistance)

IT Reactive oxygen species

RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)

(generation; \*\*\*betulinic\*\*\* acid triggers CD95 APO-1/Fas- and p53-independent apoptosis via activation of caspases in neuroectodermal tumors in relation to Bcl-2 family \*\*\*proteins\*\*\* expression and mitochondrial dysfunction and resistance)

IT Ewing's sarcoma

# Medulloblastoma

(inhibitors; \*\*\*betulinic\*\*\* acid triggers CD95 APO-1/Fas- and p53-independent apoptosis via activation of caspases in neuroectodermal tumors in relation to Bcl-2 family \*\*\*proteins\*\*\* expression and mitochondrial dysfunction and resistance)

## IT Brain tumor inhibitors

(medulloblastoma; \*\*\*betulinic\*\*\* acid triggers CD95 APO-1/Fas- and p53-independent apoptosis via activation of caspases in neuroectodermal tumors in relation to Bcl-2 family \*\*\*proteins\*\*\* expression and mitochondrial dysfunction and resistance)

## IT 169592-56-7, Caspase 3 179241-78-2, Caspase 8

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)

( \*\*\*betulinic\*\*\* acid triggers CD95 APO-1/Fas- and p53-independent apoptosis via activation of caspases in neuroectodermal tumors in relation to Bcl-2 family \*\*\*proteins\*\*\* expression and mitochondrial dysfunction and resistance)

## IT 472-15-1, \*\*\*Betulinic\*\*\* acid

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

( \*\*\*betulinic\*\*\* acid triggers CD95 APO-1/Fas- and p53-independent apoptosis via activation of caspases in neuroectodermal tumors in relation to Bcl-2 family \*\*\*proteins\*\*\* expression and mitochondrial dysfunction and resistance)

## IT 122191-40-6, Interleukin 1.beta.-converting enzyme

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

( \*\*\*betulinic\*\*\* acid triggers CD95 APO-1/Fas- and p53-independent apoptosis via activation of caspases in neuroectodermal tumors in relation to Bcl-2 family \*\*\*proteins\*\*\* expression and mitochondrial dysfunction and resistance)

## IT 9055-67-8, Poly(ADP-ribose)polymerase

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(cleavage of; \*\*\*betulinic\*\*\* acid triggers CD95 APO-1/Fas- and p53-independent apoptosis via activation of caspases in neuroectodermal tumors in relation to Bcl-2 family \*\*\*proteins\*\*\* expression and mitochondrial dysfunction and resistance)

L8 ANSWER 6 OF 9 CA COPYRIGHT 2000 ACS

AN 128:139 CA

TI Resistance to a drug blocking human immunodeficiency virus type 1 entry (RPR103611) is conferred by mutations in gp41

AU Labrosse, Beatrice; Pleskoff, Olivier; Sol, Nathalie; Jones, Christophe; Henin, Yvette; Alizon, Marc

CS INSERM, Institut Cochin de Genetique Moleculaire, Paris, 75014, Fr.

SO J. Virol. (1997), 71(11), 8230-8236

CODEN: JOVIAM; ISSN: 0022-538X

PB American Society for Microbiology

DT Journal

LA English

AB A triterpene derived from \*\*\*betulinic\*\*\* acid (RPR103611) blocks human immunodeficiency virus type 1 (HIV-1) infection and fusion of CD4+ cells with cells expressing HIV-1 envelope \*\*\*proteins\*\*\* (gp120 and gp41), suggesting an effect on virus entry. This compd. did not block infection by a subtype D HIV-1 strain (NDK) or cell-cell fusion mediated by the NDK envelope \*\*\*proteins\*\*\*. The genetic basis of drug resistance was therefore addressed by testing envelope chimeras derived from NDK and a drug-sensitive HIV-1. . . can affect the quaternary structure of gp120 and gp41 and the accessibility of gp120 to antiviral agents such as neutralizing \*\*\*antibodies\*\*\*. However, a direct effect of RPR103611 on a gp41 target must also be envisioned, in agreement with the blocking of. . .

L8 ANSWER 7 OF 9 CA COPYRIGHT 2000 ACS

AN 124:82138 CA

TI Selective inhibition of cyclic AMP-dependent protein kinase by amphiphilic triterpenoids and related compounds

AU Wang, Bing Hui; Polya, Gideon M.

CS Department Chemistry, La Trobe University, Bundoora, 3083, Australia

SO Phytochemistry (1996), 41(1), 55-63

CODEN: PYTCAS; ISSN: 0031-9422

DT Journal

LA English

IT 77-52-1, Ursolic acid 80-97-7, Dihydrocholesterol 81-23-2, Dehydrocholic acid 81-24-3, Taurocholic acid 81-25-4, Cholic acid 83-44-3, Deoxycholic acid 106-02-5, 15-Pentadecanolide 106-14-9, 12-Hydroxystearic acid 111-16-0, Pimelic acid 123-99-9, Azelaic acid, biological studies 434-13-9, Lithocholic acid 464-92-6, Asiatic acid 471-53-4, 18.beta.-Glycyrrhetic acid 472-15-1, \*\*\*Betulinic\*\*\* acid 473-98-3, Betulin 474-25-9, Chenodeoxycholic acid 475-31-0, Glycocholic acid 505-48-6, Suberic acid 508-02-1, Oleanolic acid 508-52-1, Ouabagenin 516-35-8, Taurochenodeoxycholic acid 516-50-7, Taurodeoxycholic acid 545-46-0, Uvaol 630-60-4, Ouabain 640-79-9, Glycochenodeoxycholic acid 1166-52-5, Laurylgallate 1249-75-8, Lithocholic acid methyl ester 1405-86-3 1448-36-8, Cholic acid methyl ester 1449-05-4, 18.alpha.-Glycyrrhetic acid 1679-53-4, 10-Hydroxydecanoic acid 5255-17-4 10325-79-8 16830-15-2, Asiaticoside 20231-57-6 27013-91-8, .alpha.-Hederin 27876-94-4, Crocetin p

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(selective inhibition of cAMP-dependent \*\*\*protein\*\*\* kinase by amphiphilic triterpenoids and related compds.)

L8 ANSWER 8 OF 9 CA COPYRIGHT 2000 ACS

AN 123:17583 CA

TI Constituents of Byrsonima crassifolia and their spasmogenic activity

AU Bejar, Ezra; Amarquaye, Ambrose; Che, Chun-tao; Malone, Marvin H.; Fong,



Harry H.S.

CS School of Pharmacy, University of the Pacific, Stockton, CA, 95211, USA

SO Int. J. Pharmacogn. (1995), 33(1), 25-32

CODEN: IJPYEW; ISSN: 0925-1618

DT Journal

LA English

AB . . . Byrsonima crassifolia, 22 compds. were isolated and identified from a MeOH ext. Among the isolates were six triterpenes (betunaldehyde, betulin, \*\*\*betulinic\*\*\* acid, lupeol, oleanolic acid, and ursenaldehyde), two sterols (.beta.-sitosterol and its glucoside), six flavonoids (catechin, epicatechin, guaijaverin, hyperin, quercetin and its 3-O-[6"-galloyl]galactoside), an arom. ester (Me gallate), four common amino acids (alanine, aspartic acid, proline, and valine), two non- \*\*\*protein\*\*\* amino acids (pipecolic acid and 5-hydroxypipecolic acid), and a novel sulfonoglycolipid. Biol. evaluations showed that five of these compds. (betulin, \*\*\*betulinic\*\*\* acid, hyperin, quercetin, and ursenaldehyde) exhibited spasmogenic activity on isolated rat fundus, and three isolates (hyperin, pipecolic acid and 5-hydroxypipecolic. . .

L8 ANSWER 9 OF 9 CA COPYRIGHT 2000 ACS

AN 120:289424 CA

TI Anti-AIDS agents, 11. Betulinic acid and platanic acid as anti-HIV principles from Syzigium claviflorum, and the anti-HIV activity of structurally related triterpenoids

AU Fujioka, Toshihiro; Kashiwada, Yoshiki; Kilkuskie, Robert E.; Cosentino, L. Mark; Ballas, Lawrence M.; Jiang, Jack B.; Janzen, William P.; Chen, Ih Sheng; Lee, Kuo Hsiung

CS Sch. Pharm., Univ. North Carolina, Chapel Hill, NC, 27599, USA

SO J. Nat. Prod. (1994), 57(2), 243-7

CODEN: JNPRDF; ISSN: 0163-3864

DT Journal

LA English

AB \*\*\*Betulinic\*\*\* acid (I) and platanic acid, isolated from the leaves of Syzigium claviflorum, were inhibitors of HIV replication in H9 lymphocyte. . . acid group, as well as the C-19 substituents, contribute to enhanced anti-HIV activity. The inhibitory activity of these compds. against \*\*\*protein\*\*\* kinase C (PKC) was also examd., since a correlation between anti-HIV and anti-PKC activities has been suggested. However, there was. . .